5.10 (old 3.13.10) Follow-up of Newborns with Hemoglobin Patterns A, AF, or FA Who Were Screened Only After Transfusion

GENERAL INFORMATION/POLICY: Hemoglobin and galactosemia screening results utilizing the standard newborn screening technology are invalid for three months (based on the lifespan of red blood cells) if a newborn has been transfused with whole blood or packed red blood cells prior to specimen collection. The NBS Program recommends that a transfused baby be tested for hemoglobinopathies, and offers the options of having the baby immediately tested via DNA, or testing the baby's blood three months after the last transfusion utilizing electrophoresis. The former option is preferable because outcomes for some of the hemoglobinopathies are better if treatment is initiated by two months of age. These options are noted on the baby's NBS result mailer.

Hemoglobin

- Newborns with hemoglobin patterns A, AF, or FA who were verified to have been screened only after a transfusion may be tested in the first weeks of life for some hemoglobinopathies utilizing DNA analysis. The Hemoglobinopathy Reference Lab at Children's Hospital and Research Center at Oakland (CHRCO) will perform DNA analysis on whole blood specimens of transfused babies for S,C,D,E, and O_{Arab} hemoglobin patterns and the most common beta thalassemia mutations. Babies having at least one Asian***** parent will also have testing for the six most common alpha thalassemia deletions and the Hb H Constant Spring mutation, to detect Hemoglobin H Disease, Hb H/Constant Spring, and Alpha Thalassemia Major, found almost exclusively in individuals of Asian descent.

- The group of newborns to whom this protocol refers includes those whose TRFs indicate they were screened after a transfusion, as well as those who were verified to have been screened post-transfusion even though the TRFs do not indicate such (e.g., those with an "A only" hemoglobin pattern not explained by age at specimen collection).

- The usual follow-up hemoglobin testing for non-transfused babies includes a hemogram and thin layer isoelectric focusing (electrophoresis) on the red cell fraction of whole blood. Based upon these results, additional testing may be done. In transfused babies, thin layer isoelectric focusing (electrophoresis) on the red cell fraction of whole blood and DNA testing on white blood cells will be performed.

Galactosemia

The Program recommends and offers testing through the galactosemia confirmatory laboratory, Associated Regional and Specialty Pathologists, Inc. (ARUP), when a transfused baby is suspected of having galactosemia or when there is a known family history of the disorder.

* "Asian" refers to all the ethnicities listed on the TRF except Black, Middle Eastern, Native American, Hispanic, or White

Protocol:

Resp. Person/Entity	Action
Results mailer, indicating that baby was screened post-transfusion (see attached mailer wording).	• Offers further testing for specific clinical interpretation of hemoglobin pattern. • Recommends/offers galactosemia testing (See 3.2 Galactosemia—Follow-up of Positives) if baby is suspected of having galactosemia or if there is a family history of the disorder. • Instructs primary care provider (PCP) to contact the ASC listed at the bottom of the results mailer for assistance/consultation.
ASC NBS Staff	• If a physician inquires about the initial NBS results for a baby whose results mailer stated that hemoglobin and galactosemia results were uninterpretable due to a transfusion, searches NBS computer database to ascertain if baby had been screened earlier, prior to transfusion. If this is the case, no further testing is indicated. Links the pre- and post transfusion cases in SIS. • If transfusion is indicated on the TRF with no transfusion date and time, verifies the transfusion status with the hospital. Enters correct transfusion information in the case summary in SIS. If there was no transfusion, interpretations will appear and a results mailer will be generated. **If transfusion is verified and there was no adequate pre-transfusion specimen obtained, explains the following to PCP:** **GALACTOSEMIA:** The PCP needs to assess the baby's risk for galactosemia. If there is a family history of galactosemia or if the baby is exhibiting signs of the disorder, the baby should have blood drawn for testing at ARUP, the galactosemia confirmatory laboratory (see Protocol 3.2). **HEMOGLOBINOPATHIES:** The PCP has the option of having a whole blood specimen obtained for DNA testing to rule out sickle cell disease, beta thalassemia major and other significant beta globin disorders. Babies verified by parents to have at least one Asian parent will have additional DNA testing to rule out Hemoglobin H Disease, Hb H Constant Spring and Alpha Thalassemia Major. It is optimal to have the specimen collected as soon as possible prior to discharge and before 2 months of age. **Galactosemia Follow-up:** • If PCP requests testing for galactosemia, assists with arrangements for infant's blood specimens to be collected and sent to ARUP. Faxes

ARUP manual requisition form (3.2.3) and Instructions for Collection of Samples for Galactosemia Testing (3.2.1).

Hemoglobinopathy Follow-up:

- If testing for hemoglobinopathies is requested, asks primary care provider/nursery to verify parents' ethnicity with the parents, which will be used to determine if baby's specimen should be tested for alpha thalassemia. Non-Asian babies will not be tested for alpha thalassemia, as Hemoglobin H Disease and Alpha Thalassemia Major are uncommon in non-Asians. **Ethnicity must be documented on lab intake form**. If different from the ethnicity checked on the TRF, corrects the ethnicity in SIS.

- Assists primary care provider/nursery in making arrangements to have a whole blood specimen collected to be sent to the Hemoglobin Reference Lab at CHRCO for DNA testing for hemoglobinopathies, following Protocol 5.8 (Instructions for Collection, Handling, and Mailing of Blood Specimens for Confirmatory Testing for Hemoglobinopathies). **On lab intake form, include a note about the blood products with which baby was transfused,** e.g., whole blood, packed red blood cells. ***If the baby received whole blood, parent blood specimens must also be sent to the Hemoglobin Reference Lab to obtain an accurate interpretation of the baby's hemoglobin type.***

- **Note:** If the blood specimen is obtained 3 months or more after the last transfusion, the lab intake form must note the baby's age and request electrophoresis and CBC only; alerts Hemoglobin Reference Lab that beta globin DNA testing on the specimen is not needed.
  If at least one parent is Asian, include request for alpha globin DNA testing.

- **For babies in the hospital neonatal unit**, faxes blood collection and shipping instructions, GSO express shipping label and lab intake forms to the charge nurse, nursing supervisor or neonatologist according to the hospital's preference.
  - All forms are to be sent to the hospital lab along with the blood specimen for send-out.
  - The neonatal unit faxes the completed lab intake form to the ASC when the blood has been collected.
  - Provides mailing canister to hospital lab if needed.

- If request for testing is initiated by the neonatologist **after the baby has been discharged**, obtains contact information for the primary care provider from the hospital discharge planner or Medical Records. If provider information is not available or family has changed providers, contacts the mother for the name and phone number of the provider (explains that follow-up is needed to complete the newborn screening).

	• Calls the primary care provider to arrange for follow-up. If agreed to by the PCP, assists in arranging for specimen collection at birth hospital lab or other collection site and shipping to CHRCO. • ASC notifies collection site that the infant's blood (and parents' blood if indicated) is to be drawn for NBS follow-up. Provides *Instructions for Collection, Handling, and Mailing of Confirmatory Blood Specimens,* Lab Intake form (5.8), and shipping materials (including cylinder and GSO label). • Asks lab to fax the intake form to the ASC after the blood is collected. • Sends appropriate **Doctor Letter (#36-41)** to the primary care provider. • Locates baby in SIS and enters tracking event to open case. Enters other tracking events and case notes as appropriate • **Monitors case status weekly for receipt of specimens by the Hemoglobin Reference Lab**; if notification of receipt is not received in two weeks, checks GSO shipment tracking or calls CHRCO lab to determine if specimen was received. If it wasn't, calls nursery/physician regarding transfusion follow-up and requests that MD inform the coordinator if/when specimen is collected.
Hb. Reference Lab (CHRCO)	• When specimen is received, faxes intake form with date of receipt to the referring ASC. • Performs hemoglobin electrophoresis and DNA testing for S, C, D, E, and O_{Arab} and the most common beta thalassemia mutations on all specimens of babies referred for post-transfusion hemoglobin testing. **Note:** Beta globin DNA analysis is not necessary if the infant's specimen was collected 3 months or more after the last transfusion. • Performs CBC and electrophoresis on blood specimens of parents whose babies were transfused with whole blood. • Performs DNA testing for the most common alpha thalassemia deletions (3.7 KB, 4.6 KB, 20.5 KB, SEA, FIL, THAI,) and Hb Constant Spring on all post-transfusion babies who have been verified to be Asian. • **Within 11 working days** of receipt of the sample informs ASC NBS Coordinator of the electrophoresis and beta globin DNA results by fax; sends a hard copy to the NBS Coordinator and NBSB Hb Coordinator. • **Within 31 calendar days** of receipt of the sample**,** faxes and mails reports on results the alpha globin DNA analysis for babies having at least one Asian parent.

5.10 Follow-up of Newborns with Hemoglobin Patterns A, AF, or FA Who Were Screened Only After Transfusion

ASC NBS Staff	• If baby is found to have a hemoglobinopathy, follows appropriate protocol specific to the pattern. • **If the results are negative**, sends the lab reports with **Doctor Letter #37A or 37B + C** to the nursery or primary care provider. • **If the results indicate a hemoglobin trait**, sends the appropriate **doctor letter (#38-44)** and a pamphlet about the trait for the physician to share with the family. Includes the toll-free Hemoglobin Trait Follow-up Program Number for babies identified with Sickle Cell Trait, Hb C Trait or Hb D Trait. For other trait results (unidentified Variant, alpha or beta thalassemia, or Hb E) the parents can be referred to a genetic counselor at a Sickle Cell Disease Center or Prenatal Diagnosis Center for counseling about the trait. • Enters tracking events, case notes, and resolves case in SIS. The case resolution for hb traits is “Carrier” with a note in “Comments” about the trait that was identified. • Reports any missed cases, lost to follow-up cases, delays in contacting nursery/physician or other unusual occurrences of potential significance to the NBSB Nurse Consultant. • Reports delays in analysis or reporting of confirmatory results or questions about confirmatory results to the NBSB Hemoglobin Coordinator.

